REMARKS

Claims 1- 4, 6, 9, 10, 20, 22 and 23 are active in this application in which prosecution has been opened. Reconsideration is again respectfully requested.

In an effort to conclude the prosecution of the above-identified patent application, Claims 5, 7, 8, and 11-17 are canceled, Claims 1, 6, 10 and 20 are amended to more particularly define Applicants' invention and Claims 22 and 23are newly presented for examination. Claim 1 is amended to delete language superfluous to the essential definition of the invention and recite that the first and second particles have a mean diameter of from 30 to 600 nm and that they are capable of causing light scattering at between 300 and 1,200 nm thereby being suitable for the detection of agglutinated microparticles. Support for the specific size range for the particles of the claimed reagent is found, inter alia, at page 19, line 2 of Applicants' specification.

The terms "performing" and "the amount of" in lines 1 and 2, respectively, of Claim 1 are considered redundant and are deleted. The recitation that the particles making up the subject reagent are inorganic, organic or polymeric deleted as being unnecessarily limiting of Applicants' invention since the critical characteristics of the first and second particles are the difference in light scattering properties between them, the difference in the binding partners coating them and their size, not the specific type of material comprising them. The second recitations in Claim 1, lines 13 and 14-15, respectively, that the binding partners are coated on the particles are deleted as being redundant. Finally, the language "wavelengths suitable for the detection of agglutinated microparticles" in the last line of Claim 1 is replaced with "wavelengths between 300 and 1,200 nm". Support for this language is found in Applicants' specification in the fist paragraph on page 8. It is respectfully submitted that Claim 1, as amended, is clearly patentable over the citations of record.

Claim 6 is amended to depend from Claim 1 and to remove superfluous language. The critical limitation of the claim, i.e. the concentration ratio of the first and second microparticles, is unchanged. Claim 10 is amended to replace the language "immunological binding partners' with Applicants' preferred embodiment thereof, i.e. monoclonal antibodies or fragments thereof. Support for this language is found in Applicants' specification at page 14, the paragraph

beginning at line 6, specifically line 10. Claim 20 is amended to restate lines 1 and 2 in a more preferred form without changing the substance of the Claim. Claim 22, newly submitted, is drawn to a preferred embodiment of Applicants' invention wherein the analyte to be determined using the subject reagents is a C-reactive protein and the first and second binding partners recognize different epitopes of the C-reactive protein. Support thereof is found in the paragraph beginning on line 4 of page 15 and in Example 2 of Applicants' specification. Claim 23, newly submitted, is drawn to another preferred embodiment of Applicants' invention wherein the analyte to be determined using the subject reagents is prostate specific antigen (PSA) and the first and second binding partners recognize different epitopes of PSA. Support thereof is found in line 2 of page 11 and in Example 1 of Applicants' specification. It is respectfully submitted that the Claims now under consideration define patentable subject matter over the citations of record.

Rejections under 35 U.S.C. § 102(b)

The rejection of Claims 1-3, 6, 7, 10-12 and 20, now Claims 1-3, 6, 10 and 20, under 35 U.S.C. §102 as being anticipated by *Lindmo et al.*. is respectfully controverted. The rejection as it would apply to Claims 7, 11 and 12 is obviated by their cancellation. Applicants have difficulty reconciling the fact that these Claims have progressed to the point of an Appeal Brief and only now in a subsequent Office Action have been found to be anticipated by *Lindmo et al.*. which has been of record from the beginning. A number of similarities and parallels between the teachings of *Lindmo et al.*. and the claims under consideration are proffered in the Office Action under reply. However, that is not the criteria for anticipation. *Lindmo et al.*. cannot anticipate the Claims because it fails to enable an agglutination assay. Anticipation requires that all of the elements and limitations of the claim are found within a single prior art reference See Scripps Clinic & Research Found. v. Genentech, Inc., 927 F.2d 1565, 1576, 18 USPQ2d 1001, 1010 (Fed. Cir. 1991) "There must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention." Scripps Clinic, 927 F.2d at 1576.

It is stated in the Office Action under reply that if the prior art structure is capable of performing the intended use, then it meets the claim. The converse is likewise true, if the prior

art structure is incapable of performing the intended use, i.e. an agglutination assay, it does not meet the claim. It is clear that, unlike the particles described by *Lindmo et al.*., the microparticles defined by the Claims as amended are colloidal particles suitable for agglutination assays. The particles taught by *Lindmo et al.*. are not colloidal but are "relatively large" (See *Lindmo et al.*, page 184, column 2), i.e. 7-10 μm in diameter, which renders them individually distinguishable by flow cytometry, but renders them incapable of producing meaningful results in an agglutination assay as taught by Applicants. Since the assay of *Lindmo et al.*. is based on principles unrelated to those for which the claimed reagent is suitable, the person of ordinary skill would understand that the flow cytometry reagent disclosed in *Lindmo et al.*. does not share the structural and functional characteristics of the claimed agglutination assay reagent. Thus Lindmo fails to meet the requirements of an anticipatory reference.

The Claims, as amended, define a specific particle range for both first and second microparticles that is within the range recognized by those skilled in the art as being suitable for particles used in light scattering agglutination assays . As understood by those or ordinary skill such particles are colloidal in nature. (See, e.g. Newman et al., Review Article, Ann. Clin. Biochem 1992, 22-42, page 26, of record in Applicants' IDS). Colloidal particles are within the size range of 1 nm to 1 μm "excluding those small single ions at one end and particles that do not remain dispersed by Brownian motion at the other extreme"(Id), It is recognized as stated in Applicants' specification in the first paragraph of page 8 that the particle size is chosen to be substantially smaller or slightly smaller than the wavelength utilized for detection of agglomerated microparticles (between 300 and 1200 nm), clearly excluding the particle size range of *Lindmo et al.*. (7-10 μm). There is a similar teaching at page 367 of Grange et al. The claims as amended also recite this wavelength, i.e. between 300 to 1200 nm.

A typical particle size for agglutination assays is around 300 nm (see Grange et al. cited but not relied upon in the office action under reply). This is essentially in the middle of the particle size range in the amended Claims under consideration (as presently claimed, from 30 to 600 nm). The upper limit to colloidal particle size range is commonly taken to be the size at which individual particles become visible in an optical (i.e., light) microscope (about 1 μm).

Lindmo et al.'s non-colloidal particles (7-10μm) are clearly outside the scope of the amended claims.

It is respectfully submitted that the knowledge of those skilled in the art, as clearly documented by Applicants' specification and the citations themselves is that the particles and the assay disclosed by *Lindmo et al.*. are clearly distinct from Applicants' invention. The present invention particles fall within the colloidal size range (30-600 nm). The person of ordinary skill would understand that the flow cytometry reagent disclosed in *Lindmo et al.*. does not share the structural and functional characteristics of the claimed agglutination assay reagent. In the colloidal size range of the present invention, the surface area of a particle is so much greater than its volume that unusual behavior is observed that is not observed in Lindmo's "relatively large particles, e. g., colloidal particles do not settle out by gravity (i.e., they neither float nor sink). The upper limit to colloidal particle size range is commonly taken to be the size at which individual particles become visible in an optical (i.e., light) microscope (about 1 μm), clearly excluding particles in *Lindmo et al.*'s size range (7-10μm) in which particles are individually distinguishable in a flow cytometer. Therefore, *Lindmo et al.*. does not contain every element of the claimed invention as is necessary to support anticipation.

The test for anticipation is that the "identical invention must be shown in as complete detail as is contained in the patent claim." Richardson v. Suzuki Motor Co., 868 F.2d 1226, 1236 (Fed. Cir. 1989). Further, the prior art must be enabling, and describe the claimed invention "sufficiently to have placed a person of ordinary skill in the field of the invention in possession of it." In re Spada, 911 F.2d 705, 708 (Fed. Cir. 1990). It is respectfully submitted that *Lindmo et al.*. falls woefully short of meeting these requirements. Since it has been established that *Lindmo et al.*. fails to anticipate Claim 1, it is respectfully submitted that it cannot anticipate Claims 2, 3, 6, 10 and 20 for the same reasons. Withdrawal of the rejection is in order and is respectfully requested.

Rejections under 35 U.S.C. § 103

The rejection of Claims 4, 5, 8, and 13-17 under 35 U.S.C. §103(a) as being unpatentable over *Lindmo et al.*. is also respectfully controverted. The rejection of these Claims, with the exception of Claim 4, is obviated by the cancellation thereof.

There is no basis in the art for modifying *Lindmo et al.* to meet the claimed invention. The assay disclosed by *Lindmo et al.*. is based on principles unrelated to those for which the claimed reagent is suitable. Further, based on the clear distinctions enumerated above, the assay defined in Claim 4 is clearly not enabled in any way by *Lindmo et al.*. Hence, even were there a disclosure of a ratio of mean particle diameters in *Lindmo et al.*., which there is not, such disclosure would not be enabled in the context of Applicants' agglutination assay. Clearly, since the assay taught by *Lindmo et al.*. does not involve agglutination, there would be no teaching therein from which one of ordinary skill in the art would be motivated to create particles having a particular ratio as defined in Claim 4.

There is no motivation to modify the teachings of *Lindmo et al.*. in a manner which renders the claimed subject matter obvious because 1) modification to meet the present invention would destroy the intended function of *Lindmo et al.'s* particles and 2) Lindmo teaches away from the present invention. Applicants have chosen to detail the specific limitations of their invention to emphasize that the Claims under consideration are not rendered obvious by *Lindmo et al.*. *Lindmo et al.*. discloses an assay based on principles unrelated to those that underlie utilization of the reagent of the present invention. Applicants' reagent is specific for an agglutination assay wherein the microparticles are slightly or significantly smaller than the wavelength used for detection (i.e. colloidal in size). *Lindmo et al.*. disclose a reagent in which particles are "relatively large" *Lindmo et al.*, page 184, column 2). The upper limit to the colloidal particle size range is commonly taken to be the size at which individual particles become visible in an optical (i.e., light) microscope (about 1 μm). Reducing the size of *Lindmo et al.*'s particles to Applicants' colloidal size range for use in an agglutination assay would destroy their intended function. As specifically taught in Lindmo, "all particle types must be individually distinguishable, e.g. by size in flow kilometric analysis" (*Lindmo et al.*. page 188, col. 1). Therefore, *Lindmo et al.*. does not render the Claims under consideration obvious

because it is for a different type of assay based on different principles of operation and clearly teaches away from the present invention by requiring particles individually distinguishable by flow cytometry.

In light of the amendments to the claims and the foregoing remarks, reconsideration and withdrawal of the rejection of Claims 4, 5, 8, and 13-17 under 35 U.S.C. §103(a) is respectfully requested.

The rejection of Claim 9 under 35 U.S.C. §103(a) as being unpatentable over *Lindmo et al..*, further in view of Sutton et al. is respectfully traversed. *Lindmo et al..* has been discussed above. It has been established that one of ordinary skill in the art would not be led to create the reagents of the Claims under consideration by *Lindmo et al..* because the assays described therein are based on different principles utilizing clearly distinguishable microparticles. Sutton et al. teaches specific copolymers coated on the surface of insoluble particles and having covalently bound thereto an oligonucleotide complimentary to a nucleic acid analyte. Such a teaching is respectfully submitted to be unrelated to the assay taught by *Lindmo et al..* and does not render Claim 9 unpatentable in combination therewith. Therefore, based only on the fact that Sutton et al. teaches the use of oligonucleotide capture probes for a nucleic acid analyte, which is known in the art, it is respectfully submitted that one of ordinary skill in the art would not be led to create the reagent of Claim 9 by combining the teachings of Sutton et al. with *Lindmo et al..* since neither is related to an agglutination assay and their teachings are simply not otherwise combinable. In the clear lack of an enabling teaching, withdrawal of the rejection is in order and is respectfully requested.

Although the rejection of Claim 13 under 35 U.S.C. §103(a) as being unpatentable over *Lindmo et al..* has been obviated by the cancellation thereof, in an effort to conclude the prosecution of the above-identified patent application, it will be discussed with regard to newly submitted Claims 22 and 23, each of which is directed to an agglutination assay wherein the first and second binding partners recognize different epitopes of C-reactive protein and prostate specific antigen, respectively. In the Office Action under reply, Examiner cites no reference that would provide any motivation for one skilled in the art to attempt to modify the assay described by *Lindmo et al..* to prepare an agglutination assay that operates on different principles utilizing

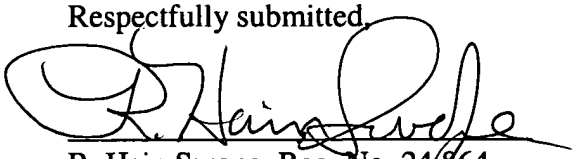
different and distinct microparticles as discussed above. If there is no teaching that would motivate one skilled in the art to attempt to modify the assay of *Lindmo et al.*., it clearly follows that refinements of the agglutination assay are not optimums within the ordinary skill of the art.

It is admitted in the Office Action under reply that *Lindmo et al.*. does not teach first and second binding partners recognizing different epitopes on an analyte. Claims 22 and 23 are directed to such limitations with the further requirement of specific analytes, i.e. C-reactive protein and prostate specific antigen, respectively. The general teaching in *Lindmo et al.*. of particles having high and low affinity in an assay referenced in the Office Action under reply is not enabling with regard to Claims 22 and 23 simply because it is a general teaching proffered in regard to a different assay that operates with different microparticles on different principles. Withdrawal of the rejection is in order and is respectfully requested.

Accordingly, it is respectfully submitted that, as Claims 1-4, 6, 9, 10, 20, 22 and 23 clearly define patentable subject matter over the citations cited of record, this application is in condition for allowance. An early Notice of Allowance is courteously solicited.

In the event the Examiner deems a further discussion of this application would expedite prosecution to allowance, the undersigned Attorney of Record would welcome the opportunity to hold such a discussion. The Examiner's cooperation in this regard would be greatly appreciated.

Respectfully submitted,



R. Hain Swope, Reg. No. 24,864
Attorney for Applicants
Phone (973) 596-4905

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Please address all communications to:
Intellectual Property Docket Administrator
Gibbons, Del Deo, Dolan, Griffinger & Vecchione
One Riverfront Plaza
Newark, New Jersey 07102-5496